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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/012,202	12/05/2001	Mark Hirsh	CP 103	5239

23579 7590 07/21/2003

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[REDACTED] EXAMINER

SHEIKH, HUMERA N

[REDACTED] ART UNIT

[REDACTED] PAPER NUMBER

1615

DATE MAILED: 07/21/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/012,202	HIRSH, MARK	
	Examiner Humera N. Sheikh	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 27 May 2003 (paper no. 9)
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-29 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-29 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) Interview Summary (PTO-413) Paper No(s). _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED ACTION

Status of the Application

Receipt of the Amendment filed 05/15/03 and the Change of Address filed 05/27/03 is acknowledged.

Claims 1-29 are pending. Claims 1-29 remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rencher et al. (US Pat. No. 5,451,409, collectively, "Rencher").

Rencher teaches a sustained release oral dosage form comprising a polymer blend of hydroxypropyl cellulose and hydroxyethyl cellulose in which one or more drugs or medicaments are combined in a single dosage form wherein each medicament is released at precise periods of time to provide the desired activity over a period of 2 to 24 hours and wherein the active medicaments include sedating antihistamines and non-sedating antihistamines and combinations thereof (see reference column 1, line 60 through col. 3, lines 67).

Rencher states that one or more medicaments may be combined in a single dosage form, depending on the chemical compatibility of the combined active ingredients and the ability to obtain the desired release rate from the dosage form for each active ingredient (col. 2, lines 47-53).

Representative types of active medicaments include, for example, anti-inflammatory drugs, analgesics, decongestants, anti-pyretics and antihistamines and wherein examples of specific active medicaments include dexbrompheniramine, chlorpheniramine and loratadine theophylline, for example (col. 3, lines 10-26).

Rencher further teaches that formulations containing NSAIDS (non-steroidal anti-inflammatory drugs) may also contain therapeutic amounts of other pharmaceutical actives, such as *decongestants* (pseudoephedrine, phenylpropanolamine), *antitussives* (caraminophen, dextromethorphan), *antihistamines*, such as chlorpheniramine, brompheniramine, dexchlorpheniramine, dexbrompheniramine, tripolidine, doxylamine,

etc and pharmaceutically acceptable salts and also non-sedating antihistamines, such as acrivastine, astemizole, cetirizine, ketotifen, loratadine, temelastine, terfenadine and combinations of any of the aforesaid pharmaceuticals (col. 3, lines 27-55).

In addition, Rencher teaches that the aforesaid pharmaceutical may be combined with acetaminophen for the treatment of allergies, cough, colds, cold-like and/or flu-like symptoms in humans. The specific preferred combination of HPC and HEC of the invention with *two or more actives* provides a single sustained release medicament, which provides the pharmacological properties of each active. Thus, repeated administration of several single component dosage forms throughout the day may be avoided (col. 3, lines 56-67).

Rencher's patent is deficient only in the sense that it does not teach the claimed release rate profiles for the sedating and non-sedating antihistamines. However, since Rencher teaches at column 2, lines 21-26, that the invention is a simple combination of one or more actives wherein *each active component* is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours, it is deemed obvious to one of ordinary skill familiar with this art to manipulate Rencher's teachings to obtain the desired release profile for each of the drugs in the combination.

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Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al. (US Pat. No. 5,827,852, collectively, "Russell") in view of Rencher et al. (US Pat. No. 5,451,409, collectively, "Rencher").

Russell teaches coated pharmaceutical compositions for oral administration comprising pharmaceutical actives for treating cold, cough, cold-like, allergy and/or flu symptoms, wherein the active ingredients include sedating antihistamines and non-sedating antihistamines and mixtures thereof (see reference column 5, line 33 through col. 6, line 25 and claim 7).

Russell teaches that the actives which can be used are for example sedating antihistamines, such as chlorpheniramine, brompheniramine, dexchlorpheniramine, dexbrompheniramine, tripolidine, azatadine, doxylamine, tripelennamine, cyproheptadine, hydroxyzine, clemastine, etc and their pharmaceutically acceptable salts and also non-sedating antihistamines, which include acrivastine, astemizole, azelastine, cetirizine, ebastine, ketotifen, Iodoxamide, loratadine, temelastine, etc and pharmaceutically acceptable salts (col. 6, lines 5-15).

Additional pharmaceutical actives are those having analgesic, anti-inflammatory, anesthetic, decongestant, cough suppressant, antitussive and/or expectorant properties (col. 5, lines 34-42).

Russell states that various oral dosage forms suitable for coating can be used, including solid forms as tablets, capsules, pills and lozenges. The tablets can be compressed, molded, enteric-coated, sugar-coated, film-coated or multiple compressed (col. 3, line 54 through col. 4, line 14).

Russell is deficient only in the sense that he does not explicitly teach separate release profiles for the sedating and non-sedating antihistamines.

Rencher, as discussed above, teaches at column 2, lines 21-26 that the invention is a simple combination of one or more actives wherein *each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours*.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Rencher within the teachings of Russell because Rencher explicitly teaches a combination of one or more actives wherein each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours, thus avoiding repeated administration. The expected result would be an improved, single dosage formulation providing separate release profiles for each of the drugs in the combination, as similarly desired by the applicant.

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitra (US Pat. No. 5,648,358) in view of Rencher et al. (US Pat. No. 5,451,409, collectively, “Rencher”).

Mitra teaches antihistamine compositions and methods for providing improved treatment, management or mitigation of cold, cold-like, allergy, sinus and/or flu

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symptoms, wherein the composition comprises caffeine, pyrroline and piperidine ether antihistaminic agents, which contain a sedating antihistamine, preferably clemastine fumarate and can also include an additional sedating antihistamine and a non-sedating antihistamine and mixtures thereof (see reference column 2, line 6 through col. 3, line 53 and claims).

Mitra teaches that the composition can include at least one other pharmaceutical active selected from: a decongestant, expectorant, an additional antihistamine, an antitussive, etc. The additional antihistamine include those sedating antihistamines, such as chlorpheniramine, brompheniramine, dexchlorpheniramine, azatadine, triprolidine, etc and their pharmaceutically acceptable salts as well as the *non-sedating antihistamines*, which include acrivastine, astemizole, azatadine, azelastine, cetirizine, loratadine, temelastine, etc. and their pharmaceutically acceptable salts and mixtures thereof (col. 3, lines 1-27).

Additionally, Mitra states that various oral dosage forms can be used, including tablets, caplets, capsules, granules, lozenges and the like. Tablets can be compressed, enteric-coated, sugar-coated, film-coated, or multiple compressed. Mitra teaches that controlled release dosage forms, which provide a controlled release of these active(s) are also useful (col. 3, lines 40-58).

Mitra is lacking only in the sense that he does not teach separate release profiles for the sedating and non-sedating antihistamines.

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Rencher, as discussed above, teaches at column 2, lines 21-26 that the invention is a simple combination of one or more actives wherein *each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours*.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of *Rencher* within the teachings of *Mitra* because *Rencher* explicitly teaches a simple combination of one or more actives wherein each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours. The expected result would be an improved, single dosage formulation providing separate release profiles for each of the drugs in the combination, as similarly desired by the applicant.

Response to Arguments

Applicant's arguments filed 05/15/03 have been fully considered but they are not persuasive.

Firstly, the applicant argued over the 35 USC 103(a) rejection of *Rencher* ('409), stating, "Rencher fails to make obvious the claimed subject matter because Rencher does not teach (1) delayed release and (2) does not recognize the benefit of a formulation of both a sedating antihistamine and a non-sedating antihistamine, which are released at different time periods. Rencher is not particularly drawn to the delivery

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of antihistamines. Sedating antihistamine is not a concern. Rencher does not provide the motivation for one of ordinary skill in the art to make and use the claimed composition. Rencher teaches making a homogeneous composition of the active, whereas in contrast, a biphasic composition as defined in any of claims 1-29 is necessary to achieve the instant release profile. Claims 1-29 are not *prima facie* obvious over Rencher."

These arguments have been fully considered, but were not found to be persuasive. Rencher teaches a sustained release oral dosage form comprising a polymer blend of hydroxypropyl cellulose and hydroxyethyl cellulose in which one or more drugs or medicaments are combined in a single dosage form wherein each medicament is released at precise periods of time to provide the desired activity over a period of 2 to 24 hours and wherein the active medicaments include sedating antihistamines and non-sedating antihistamines and combinations thereof (see reference column 1, line 60 through col. 3, lines 67). Rencher suggests the combination of active medicaments depend on the chemical compatibility of the combined active ingredients and the ability to obtain the desired release rate from the dosage form for each active ingredient (col. 2, lines 47-53). The applicant's argument that Rencher does not recognize the benefits of sedating and non-sedating antihistamines and is not drawn to antihistamines is disagreed upon since the prior art desires the incorporation of active medicaments, particularly, sedating and non-sedating antihistamines combined in a single formulation tablet as claimed in claims 5 and 6 of the '409 patent. The art further exemplifies the use of specific antihistamines in the examples at columns 5-10.

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The art also teaches or suggests that the active components are released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours. As such, the prior art would also recognize the advantages or benefits that arise from sedative and non-sedative compositions. Rencher provides ample motivation for one of ordinary skill in the art to make and/or use the invention. The argument that Rencher does not teach a delayed release form is not seen as persuasive, since Rencher does suggest a controlled release formulation whereby the active components are released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours. Furthermore, the actives are chosen so that they are released at even precise periods of time. One of ordinary skill in this art could conduct routine or manipulative experimentations to arrive at the best possible results for appropriate or desired release rates. The claims are *prima facia* obvious in view of Rencher since the prior art clearly teaches a formulation comprising both sedative and non-sedative antihistamines and further includes specific antihistamines as instantly claimed. Therefore, the instant invention is rendered obvious and unpatentable over the art.

Secondly, the applicant argued over the rejection of Russell ('852) in view of Rencher stating, "The composition of Russell would not delay the release of any of the active ingredients. Russell in combination with Rencher fails to teach one skilled in the art to (1) make a biphasic composition; (2) for delivery of a sedating antihistamine during the night and a non-sedating antihistamine during the daytime. Accordingly, Russell in view of Rencher would not render the claims *prima facia* obvious."

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These arguments have been fully considered, but were not found to be persuasive. Russell teaches coated pharmaceutical compositions for oral administration comprising sedating antihistamines and non-sedating antihistamines and mixtures thereof (col. 5, line 33 through col. 6, line 25 and claim 7). Russell is lacking the sense that he does not teach separate release profiles for the sedating and non-sedating antihistamines. Rencher was relied upon solely for the teaching that it is obvious to formulate one or more actives having specific release rates and particularly, as taught in col. 2, lines 21-26, wherein *each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours*. Rencher explicitly teaches sedating and non-sedating antihistamines, as does Russell. One of ordinary skill in the pharmaceutical art incorporating sedative and non-sedative antihistamine formulations would also recognize the advantages associated with the combined use of sedating (nighttime) and non-sedating (daytime) antihistamines. Hence, Russell in view of Rencher is viewed as being *prima facia* obvious.

Lastly, the applicant argued over the rejection of Mitra ('358) in view of Rencher, stating, "Mitra in combination with Rencher fails to teach or make obvious a biphasic composition for delivery of a sedating antihistamine in the night and a non-sedating antihistamine in the daytime. Mitra and Rencher teach away from the claimed invention and Mitra in view of Rencher would not render claims 1-29 *prima facia* obvious."

These arguments have been fully considered, but were not found to be persuasive. Mitra teaches antihistamine compositions and methods for providing

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improved treatment, management or mitigation of cold, cold-like, allergy, sinus and/or flu symptoms, wherein the composition comprises caffeine, pyrroline and piperidine ether antihistaminic agents, which contain a sedating antihistamine, preferably clemastine fumarate and can also include an additional sedating antihistamine and a non-sedating antihistamine and mixtures thereof (see reference column 2, line 6 through col. 3, line 53 and claims). Mitra recites an array of various sedative and non-sedative antihistamines suitable for the formulation. Mitra is deficient in that he does not teach separate release profiles for the sedating and non-sedating antihistamines. Rencher was relied upon and resolves the only deficiency of Mitra because Rencher teaches one or more actives wherein *each active component is released at an appropriate rate to provide the desired activity over a period of 2 to 24 hours*. The actives taught by Rencher are sedating and non-sedating antihistamines. A *prima facia* case of obviousness is established since the prior art clearly teaches an antihistaminic composition comprising both sedating as well as non-sedating antihistamines and their mixtures. As such, the instant invention is rendered obvious and unpatentable over the cited art references.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

hns
July 18, 2003

TP
THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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